IT IS CLAIMED:

1. A conjugate having the general structure I:

$$P—L—CR^1R^2—S\text{-}S—Ar—CR^3R^4—Y—X^3—R^5$$

I

wherein:

P is a hydrophilic polymer and L is a linker moiety;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of H, alkyl, aralkyl and aryl;

Ar is an aromatic group to which S-S and CR^3R^4 are linked in a configuration which promotes rapid cleavage of the CR^3R^4—Y bond, via a 1,4-, 1,6- or related elimination reaction involving the bonds of the aromatic group, following cleavage of the S-S bond;

Y is a direct bond or $-X^1-(C=X^2)-$, where X^1 and X^2 are independently O or S; and

X^3R^5 is a ligand derived from an amine-, hydroxy- or carboxyl-containing compound, such that X^3 is an oxygen or secondary or tertiary nitrogen atom.

2. The conjugate of claim 1, wherein Ar is selected from

(i) an aromatic hydrocarbon or a ring nitrogen-containing analog thereof, to which groups S-S and CR^3R^4 are linked in such a configuration that they are separated by an odd number of peripheral ring bonds;

(ii) a 5-membered heteroaromatic ring selected from 2,4-imidazolyl, 2,4-thiazolyl, 2,4-oxazolyl, 2,5-pyrrolyl, 2,5-furanyl, and 2,5-thiophenyl, and

(iii) a polycyclic aromatic group containing a 5-membered heteroaromatic ring, to which groups S-S and CR^3R^4 are linked in such a configuration that they are separated by a path containing an odd number of peripheral ring bonds, with the proviso that said path does not include an oxygen, sulfur, or trisubstituted nitrogen ring atom.

3. The conjugate of claim 1, wherein the linker moiety L is a direct bond, amine, amide, carbamate, ether, or a carbon chain, where the carbon chain may

have one or more functional groups selected from amine, amide, carbamate, and ether, at either terminus of the chain or intervening between carbon atoms of the chain.

4. The conjugate of claim 2, wherein Ar is selected from 1,2-phenyl, 1,4-phenyl, 1, 7-napthyl, 2,9-anthracyl, and 4,5-phenanthracyl.

5. The conjugate of claim 4, wherein Ar is selected from 1,2-phenyl and 1,4-phenyl.

6. The conjugate of claim 1, wherein Y is O(C=O), and the ligand is derived from an amine-containing compound.

7. The conjugate of claim 1, wherein R^1 is H and R^2 is selected from the group consisting of CH_3, C_2H_5 and C_3H_7.

8. The conjugate of claim 1, wherein the ligand is derived from a polypeptide, an amine-containing drug, or an amine-containing lipid.

9. The conjugate of claim 8, wherein the amine-containing lipid is a phospholipid having a double hydrocarbon tail.

10. The conjugate of claim 1, wherein each of R^1 and R^2 is alkyl.

11. The conjugate of claim 1, wherein the hydrophilic polymer P is selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropyl-methacrylamide, polymethacrylamide, polydimethyl-acrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethylene glycol, polyaspartamide, copolymers thereof, and polyethylene oxide-polypropylene oxide.

12. The conjugate of claim 11, wherein P is polyethylene glycol.

13. The conjugate of claim 12, wherein R^1 is H and R^2 is CH_3, C_2H_5, or C_3H_7.

14. The conjugate of claim 1, wherein the ligand is derived from a polypeptide.

15. The conjugate of claim 14, wherein the polypeptide is a recombinant polypeptide.

16. The conjugate of claim 11, wherein the polypeptide is a recombinant polypeptide.

17. The conjugate of claim 14, wherein the polypeptide is a cytokine.

18. The conjugate of claim 14, wherein the polypeptide is selected from the group consisting of interferons, interleukins, growth factors, erythropoietin, and enzymes.

19. The conjugate of claim 14, comprising multiple hydrophilic polymers attached to said polypeptide, each by a linkage represented by $L—CR^1R^2—S\text{-}S—Ar—CR^3R^4—Y$ in structure I.

20. The conjugate of claim 11, wherein said hydrophilic polymer includes a targeting moiety at its free terminus.

21. A composition comprising, in a pharmaceutically acceptable carrier, a conjugate obtainable by reaction of an amine-, hydroxy- or carboxyl-containing compound with a compound having the general structural formula:

$$P—L—CR^1R^2—S\text{-}S—Ar—CR^3R^4—Y—R^6$$

II

wherein

P is a hydrophilic polymer and L is a linker moiety;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of

H, alkyl, aralkyl and aryl;

Ar is an aromatic group to which S-S and CR^3R^4 are linked in a configuration which promotes rapid cleavage of the CR^3R^4—Y bond, via a 1,4-, 1,6- or related elimination reaction involving the bonds of the aromatic group, following cleavage of the S-S bond;

Y is a direct bond or $-X^1-(C=X^2)-$, where X^1 and X^2 are independently O or S; and

R^6 is a leaving group.

22. The composition of claim 21, wherein Ar is selected from

(i) an aromatic hydrocarbon or a ring nitrogen-containing analog thereof, to which groups S-S and CR^3R^4 are linked in such a configuration that they are separated by an odd number of peripheral ring bonds;

(ii) a 5-membered heteroaromatic ring selected from 2,4-imidazolyl, 2,4-thiazolyl, 2,4-oxazolyl, 2,5-pyrrolyl, 2,5-furanyl, and 2,5-thiophenyl, and

(iii) a polycyclic aromatic group containing a 5-membered heteroaromatic ring, to which groups S-S and CR^3R^4 are linked in such a configuration that they are separated by a path containing an odd number of peripheral ring bonds, with the proviso that said path does not include an oxygen, sulfur, or trisubstituted nitrogen ring atom.

23. The composition of claim 22, wherein the linker moiety L is a direct bond, amine, amide, carbamate, ether, or a carbon chain, where the carbon chain may have one or more functional groups selected from amine, amide, carbamate, and ether, at either terminus of the chain or intervening between C atoms of the chain.

24. The composition of claim 22, wherein Ar is selected from 1,2-phenyl, 1,4-phenyl, 1, 7-napthyl, 2,9-anthracyl, and 4,5-phenanthracyl.

25. The composition of claim 24, wherein Ar is selected from 1,2-phenyl and 1,4-phenyl.

26. The composition of claim 21, wherein Y is O(C=O), and the compound is formed by reaction with a ligand derived from an amine-containing compound.

27. The composition of claim 21, wherein R^1 is H and R^2 is selected from the group consisting of CH_3, C_2H_5 and C_3H_7.

28. The composition of claim 21, wherein Y is O(C=O) and R^6 is a hydroxy- or oxy-containing leaving group.

29. The composition of claim 21, wherein the leaving group is derived from a compound selected from the group consisting of chloride, *para*-nitrophenol, *ortho*-nitrophenol, N-hydroxy-tetrahydrophthalimide, N-hydroxysuccinimide, N-hydroxy-glutarimide, N-hydroxynorbornene-2,3-dicarboxyimide, 1-hydroxybenzotriazole, 3-hydroxypyridine, 4-hydroxypyridine, 2-hydroxypyridine, 1-hydroxy-6-trifluoromethylbenzotriazole, immidazole, triazole, N-methyl-imidazole, pentafluorophenol, trifluorophenol and trichlorophenol.

30. The composition of claim 21, wherein the amine-containing compound comprises a phospholipid.

31. The composition of claim 30, wherein P is selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropyl-methacrylamide, polymethacrylamide, polydimethylacrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethylene glycol, polyaspartamide, copolymers thereof, and polyethyleneoxide-polypropylene oxide.

32. The composition of claim 30, wherein P comprises polyethylene glycol.

33. The composition of claim 30, wherein the composition containing the conjugate comprises a liposome.

34. The composition of claim 33, wherein the liposome further comprises an entrapped therapeutic agent.

35. The composition of claim 21, wherein the amine-containing compound comprises a polypeptide.

36. The composition of claim 35, wherein P is selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropyl-methacrylamide, polymethacrylamide, polydimethyl-acrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethylene glycol, polyaspartamide, copolymers thereof, and polyethyleneoxide-polypropylene oxide.

37. The composition of claim 35, wherein P comprises polyethylene glycol.

38. The composition of claim 37, wherein the polypeptide comprises a recombinant polypeptide.

39. The composition of claim 37, wherein the polypeptide comprises a cytokine.

40. The composition of claim 37, wherein the polypeptide is selected from the group consisting of interferons, interleukins, growth factors, erythropoietin, and enzymes.

41. A liposome composition comprising vesicle-forming lipids and having a surface coating of hydrophilic polymers, wherein at least a portion of the lipids have the general structure:

$$P—L—CR^1R^2—S\text{-}S—Ar—CR^3R^4—Y—X^3—R^5$$

I

wherein:

P is a hydrophilic polymer and L is a linker moiety;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of H, alkyl, aralkyl and aryl;

Ar is an aromatic group to which S-S and CR^3R^4 are linked in a configuration which promotes rapid cleavage of the CR^3R^4—Y bond, via a 1,4-, 1,6- or related elimination reaction involving the bonds of the aromatic group, following cleavage of the S-S bond;

Y is a direct bond or $-X^1-(C=X^2)-$, where X^1 and X^2 are independently O or S; and

X^3R^5 is a ligand derived from an amine-, hydroxy- or carboxyl-containing lipid, such that X^3 is an oxygen or secondary or tertiary nitrogen atom.

42. The composition of claim 41, wherein Ar is selected from

(i) an aromatic hydrocarbon or a ring nitrogen-containing analog thereof, to which groups S-S and CR^3R^4 are linked in such a configuration that they are separated by an odd number of peripheral ring bonds;

(ii) a 5-membered heteroaromatic ring selected from 2,4-imidazolyl, 2,4-thiazolyl, 2,4-oxazolyl, 2,5-pyrrolyl, 2,5-furanyl, and 2,5-thiophenyl, and

(iii) a polycyclic aromatic group containing a 5-membered heteroaromatic ring, to which groups S-S and CR^3R^4 are linked in such a configuration that they are separated by a path containing an odd number of peripheral ring bonds, with the proviso that said path does not include an oxygen, sulfur, or trisubstituted nitrogen ring atom.

43. The composition of claim 41, wherein the linker moiety L is a direct bond, amine, amide, carbamate, ether, or a carbon chain, where the carbon chain may have one or more functional groups selected from amine, amide, carbamate, and ether, at either terminus of the chain or intervening between C atoms of the chain.

44. The composition of claim 42, wherein Ar is selected from 1,2-phenyl, 1,4-phenyl, 1, 7-napthyl, 2,9-anthracyl, and 4,5-phenanthracyl.

45. The composition of claim 44, wherein Ar is selected from 1,2-phenyl and 1,4-phenyl.

46. The composition of claim 41, wherein Y is O(C=O), and the ligand is derived from an amine-containing lipid.

47. The composition of claim 41, wherein R^1 is H and R^2 is selected from the group consisting of H, CH_3, C_2H_5 and C_3H_7.

48. The composition of claim 41, wherein R^1 is H and R^2 is selected from the group consisting of CH_3, C_2H_5 and C_3H_7.

49. The composition of claim 46, wherein the amine-containing lipid is a phospholipid.

50. The composition of claim 41, wherein P is selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropyl-methacrylamide, polymethacrylamide, polydimethyl-acrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethylene glycol, polyaspartamide, copolymers thereof, and polyethylene oxide-polypropylene oxide.

51. The composition of claim 50, wherein P comprises polyethylene glycol.

52. The composition of claim 41, wherein the liposome further comprises an entrapped therapeutic agent.

53. The composition of claim 41, further comprising vesicle-forming lipids stably linked to a hydrophilic polymer, wherein the total mole percent of lipids linked to a hydrophilic polymer is between 1% and about 20%.

54. The composition of claim 53, wherein hydrophilic polymers stably linked to vesicle-forming lipids are shorter than those contained in the conjugates of structure I.

55. The composition of claim 53, wherein at least a portion of the hydrophilic polymers include a targeting moiety at the free terminus.

56. A method for improving the blood circulation lifetime of liposomes having a surface coating of releasable hydrophilic polymer chains, comprising

preparing liposomes that include between about 1 to about 20 mole % of lipids conjugated to a hydrophilic polymer, wherein at least a portion of said conjugated lipids have the general structure:

$$P—L—CR^1R^2—S\text{-}S—Ar—CR^3R^4—Y—X^3—R^5$$

I

wherein:

P is a hydrophilic polymer and L is a linker moiety;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of H, alkyl, aralkyl and aryl;

Ar is an aromatic group to which S-S and CR^3R^4 are linked in a configuration which promotes rapid cleavage of the CR^3R^4—Y bond, via a 1,4-, 1,6- or related elimination reaction involving the bonds of the aromatic group, following cleavage of the S-S bond;

Y is a direct bond or $-X^1-(C=X^2)-$, where X^1 and X^2 are independently O or S; and

X^3R^5 is a ligand derived from an amine-, hydroxy- or carboxyl-containing lipid, such that X^3 is an oxygen or secondary or tertiary nitrogen atom.

57. The method of claim 56, wherein Ar is selected from

(i) an aromatic hydrocarbon or a ring nitrogen-containing analog thereof, to which groups S-S and CR^3R^4 are linked in such a configuration that they are separated by an odd number of peripheral ring bonds;

(ii) a 5-membered heteroaromatic ring selected from 2,4-imidazolyl, 2,4-thiazolyl, 2,4-oxazolyl, 2,5-pyrrolyl, 2,5-furanyl, and 2,5-thiophenyl, and

(iii) a polycyclic aromatic group containing a 5-membered heteroaromatic ring, to which groups S-S and CR^3R^4 are linked in such a configuration that they

are separated by a path containing an odd number of peripheral ring bonds, with the proviso that said path does not include an oxygen, sulfur, or trisubstituted nitrogen ring atom.

58. The method of claim 56, wherein the linker moiety L is a direct bond, amine, amide, carbamate, ether, or a carbon chain, where the carbon chain may have one or more functional groups selected from amine, amide, carbamate, and ether, at either terminus of the chain or intervening between C atoms of the chain.

59. The method of claim 57, wherein Ar is selected from 1,2-phenyl, 1,4-phenyl, 1, 7-napthyl, 2,9-anthracyl, and 4,5-phenanthracyl.

60. The method of claim 59, wherein Ar is selected from 1,2-phenyl and 1,4-phenyl.

61. The method of claim 56, wherein Y is O(C=O), and the ligand is derived from an amine-containing compound.

62. The method of claim 56, wherein R^5 is H and R^2 is selected from the group consisting of H, CH_3, C_2H_5 and C_3H_7.

63. The method of claim 62, wherein R^5 is H and R^2 is selected from the group consisting of CH_3, C_2H_5 and C_3H_7.

64. The method of claim 56, wherein the amine-containing lipid is a phospholipid.

65. The method of claim 64, wherein P is selected from the group consisting of polyvinylpyrrolidone, polyvinylmethylether, polymethyloxazoline, polyethyloxazoline, polyhydroxypropyloxazoline, polyhydroxypropyl-methacrylamide, polymethacrylamide, polydimethyl-acrylamide, polyhydroxypropylmethacrylate, polyhydroxyethylacrylate, hydroxymethylcellulose, hydroxyethylcellulose, polyethylene glycol, polyaspartamide, copolymers thereof, and polyethyleneoxide-polypropylene oxide.

66. The method of claim 65, wherein P comprises polyethylene glycol.

67. The method of claim 56, wherein the liposome further comprises an entrapped therapeutic agent.

68. The method of claim 56, wherein said liposomes include vesicle-forming lipids stably linked to a hydrophilic polymer.

69. The method of claim 68, wherein hydrophilic polymers stably linked to vesicle-forming lipids are shorter than those contained in the conjugates of structure I.

70. The method of claim 56, wherein at least a portion of the hydrophilic polymers include a targeting moiety at the free terminus.

71. A polypeptide having a surface coating of hydrophilic polymer chains, wherein at least a portion of the polymer chains have the general structure:

$$P—L—CR^1R^2—S\text{-}S—Ar—CR^3R^4—Y—X^3—R^5$$

I

wherein:

P is a hydrophilic polymer and L is a linker moiety;

R^1, R^2, R^3 and R^4 are independently selected from the group consisting of H, alkyl, aralkyl and aryl;

Ar is an aromatic group to which S-S and CR^3R^4 are linked in a configuration which promotes rapid cleavage of the CR^3R^4—Y bond, via a 1,4-, 1,6- or related elimination reaction involving the bonds of the aromatic group, following cleavage of the S-S bond;

Y is a direct bond or $-X^1-(C=X^2)-$, where X^1 and X^2 are independently O or S; and

X^3R^5 is a ligand derived from an amine-, hydroxy- or carboxyl-containing polypeptide, such that X^3 is an oxygen or secondary or tertiary nitrogen atom.

72. The polypeptide of claim 71, wherein R^1 is H and R^2 is CH_3, C_2H_5, or C_3H_7.

73. The polypeptide of claim 71, wherein P is polyethylene glycol.

74. The polypeptide of claim 71, wherein the polypeptide is a recombinant polypeptide.

75. The polypeptide of claim 71, wherein, wherein the polypeptide is a cytokine.

76. The polypeptide of claim 71, wherein the polypeptide is selected from the group consisting of interferons, interleukins, growth factors, erythropoietin, and enzymes.